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Abnormalities of the Heart and Great Arteries in First Trimester Chromosomally Abnormal Fetuses

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Pathological examination of the heart and great arteries was performed in 112 chromosomally abnormal fetuses after surgical termination of pregnancy at 11–16 weeks of gestation. The chromosomal abnormalities were diagnosed by chorion villus sampling which was carried out because screening of the pregnancies by a combination of maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation identified them as being at increased risk. The group consisted of 60 fetuses with trisomy 21, 29 with trisomy 18, 17 with trisomy 13 and 6 with Ullrich-Turner syndrome. The most common cardiac lesion seen in trisomy 21 fetuses was an atrioventricular or ventricular septal defect. Trisomy 18 was associated with ventricular septal defects and/or polyvalvular abnormalities. In trisomy 13, there were atrioventricular or ventricular septal defects, valvular abnormalities, and either narrowing of the isthmus or truncus arteriosus. Ullrich-Turner syndrome was associated with severe narrowing of the whole aortic arch. In all four groups of chromosomally abnormal fetuses, the aortic isthmus was significantly narrower than in normal fetuses and the degree of narrowing was significantly greater in fetuses with high nuchal translucency thickness. It is postulated that narrowing of the aortic isthmus may be the basis of increased nuchal translucency thickness in all four chromosomal abnormalities. Am. J. Med. Genet. 69:207–216, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: aortic isthmus; cardiac defects; nuchal translucency; prenatal diagnosis; chromosomal abnormalities

INTRODUCTION

At 10–14 weeks of gestation, 80% of chromosomally abnormal fetuses have increased accumulation of subcutaneous edema in the neck, which is visualized by ultrasonography as nuchal translucency (Fig. 1) [Nicolaides et al., 1994; Pandya et al., 1995].

A series of pathological studies in both chromosomally abnormal and normal fetuses with increased nuchal translucency thickness have demonstrated abnormalities of the heart and great arteries that may be the underlying mechanism for the edema. A study of 36 trisomy 21 fetuses reported that 56% had an atrioventricular or ventricular septal defect [Hyett et al., 1995a]. Similarly, ventricular septal defects and/or polyvalvular abnormalities were found in all 19 trisomy 18 fetuses that were examined [Hyett et al., 1995b]. Furthermore, examination of the great arteries in 34 trisomy 21 fetuses demonstrated narrowing of the aortic isthmus and an increase in the ratio of the diameter of the isthmus to that of the ductus arteriosus [Hyett et al., 1995c,d].

This extended study reports the prevalence of abnormalities of the heart and great arteries in 112 fetuses with trisomies 21, 18, or 13 and Ullrich-Turner syndrome (UTS) and examines the possible association with increased nuchal translucency thickness.

MATERIALS AND METHODS

Pathological examination of the heart and great arteries was performed in 112 chromosomally abnormal fetuses (60 with trisomy 21, 29 with trisomy 18, 17 with trisomy 13, and 6 with UTS) after elective surgical termination of pregnancy at 11–16 weeks of gestation. The chromosomal abnormalities were diagnosed by chorion villus sampling, which was carried out because screening by a combination of maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation

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Fig. 1. An ultrasound image of a fetus of 12 weeks gestation showing the measurement of fetal nuchal translucency. The measurement of 3 mm increases the risk of a chromosomal abnormality above the background risk based upon maternal age.

identified these pregnancies as being at increased risk [Nicolaides et al., 1994; Pandya et al., 1995]. The study was approved by our hospital Ethics Committee and tissue collection was made in accordance with the Polkinghorne [1989] guidelines on the research use of fetal material.

Pathological Examination

In 106 pregnancies, termination was by dilatation and evacuation and in 6 by induction of labor. In each case an attempt was made to identify the heart and great arteries. The specimens were fixed by direct perfusion-inflation with 4% paraformaldehyde, injected through the apex of each ventricle under microscopic control using a low-pressure, high-flow perfusion technique [Moscoso et al., 1990]. Each specimen was fixed by simple immersion for a further 3 hours and then rinsed and stored at 4°C in sucrose phosphate buffer.

The heart was examined under a monocyclops dissecting microscope (Karl Zeiss, Oberkochen, Germany) using co-axial illumination. The atria were excised and the ventricles were divided into three segments; right parietal, septal, and left parietal by step-wise microdissection, allowing examination of the internal surface of both ventricles, the atrioventricular valves and the semilunar valves [Pexieder and Janeck, 1984].

Prior to microdissection of the heart, the external diameter of the aorta was measured immediately above the aortic valve (AoV) and at the level of the isthmus (Aol), and the pulmonary trunk was measured immediately above the pulmonary valve (PV) and at the level of the distal ductus arteriosus (Dad) as previously described [Hyett et al., 1995c].

Statistical Analysis

Each measurement of the great arteries and their ratios was expressed as a delta value, which is the number of standard deviations by which the measurement differs from the appropriate normal mean for gestational age [Hyett et al., 1995c]. A Mann Whitney test was used to determine the significance of the difference of the mean delta value from zero. Regression analysis was used to determine the significance of the association between delta values for each diameter and nuchal translucency thickness.

RESULTS

The heart was successfully recovered from 100 of the 112 cases and the great arteries in 96 cases. In 87 of the cases, the great arteries were complete, allowing all four measurements; in 9 cases there was fragmentation of the great arteries and only 23 of the possible 36 measurements were made.

Trisomy 21 (n = 60)

A ventricular or atrioventricular septal defect was detected in 24 of the 54 (44%) hearts available for examination (Table I, Fig. 2). The prevalence of septal defects increased with translucency thickness from 13% (2 of 16) for translucency of 1.0–3.4 mm to 53% (21 of 40) for translucency of 3.5 mm or more. In two cases, both with translucency of 5 mm, the perimembranous ventricular septal defect was partly obliterated by the overlying septal leaflet of the tricuspid valve (Fig. 3). Valvular abnormalities were observed in 7 (13%) of the cases, and in 4 of these the abnormality was a bicuspid aortic valve.

The great arteries were available for examination in 52 cases. The significant differences from normal were a decrease in Aol (Fig. 4), increase in AoV and increase in the ratios of AoV to PV, AoV to AoI, and Dad to AoI (Table II, Fig. 5). The prevalence of AoI below the 5th centile was 0% (none of 12) for those with translucency thickness of 1.0–3.4 mm and 55% (22 of 40) for translucency of 3.5 mm or more.

Trisomy 18 (n = 29)

Cardiac abnormalities were found in all 23 cases where the heart was available for examination. The commonest abnormalities were ventricular septal defects in 19 (83%), usually perimembranous, and valvular defects that affected more than one valve in 19 (83%) of the cases (Table III, Fig. 6).

The great arteries were available for examination in 27 cases. The significant differences from normal were decrease in AoI and increase in AoV to AoI ratio (Table II, Fig. 5). The prevalence of AoI below the 5th centile increased with translucency thickness from 0% (none of 5) for translucency of 1.0–3.4 mm to 36% (8 of 22) for translucency of 3.5 mm or more. In three of the cases with translucency > 7 mm, there was hypoplasia of the pulmonary trunk (Fig. 7) in association with an imperforate pulmonary valve. In seven cases there was persistence of the left superior vena cava draining into a dilated coronary sinus.

Trisomy 13 (n = 17)

Abnormalities of the heart were found in 15 of the 16 hearts that were available for examination and the most common were ventricular septal defects and a variety of valvular defects, including agenesis of the

TABLE I. Prevalence of Septal Defects, Valvular Abnormalities, and Narrowing of the Aortic Isthmus in Trisomy 21 Fetuses in Relation to Nuchal Translucency Thickness at Diagnosis*

Nuchal translucency	n	Septal defect		Valvular abnormalities	Aortic isthmus <5th centile
		Atrioventricular	Ventricular		
1.0–2.4 mm	4	—	—		0/4
2.5–3.4 mm	12	1	1	Bicuspid aortic valve (2) Dysplastic tricuspid valve	0/8
3.5–4.4 mm	9	2	2	Bicuspid pulmonary valve	4/9
4.5–5.4 mm	13	4	3	Bicuspid aortic valve (2)	10/13
5.5–6.4 mm	3	1	—		2/3
6.5–7.4 mm	3	2	—	Bicuspid pulmonary valve	1/3
7.5–8.4 mm	5	2	2		4/5
8.5–9.4 mm	3	—	1		2/3
9.5–10.4 mm	2	1	—		2/2
10.5–14.0 mm	2	—	1		1/2

* Denominator is the number of cases examined.

pulmonary valve that was not observed in the other chromosomal abnormalities (Table IV).

The great arteries were available for examination in 15 cases and abnormalities were observed in all cases. The significant differences from normal were decrease in both AoV and AoI and an increase in the ratios of AoV to AoI and of Dad to AoI (Table II, Fig. 5). Truncus arteriosus (Fig. 8) was found in 3 (20%) cases, and this was also a finding unique to trisomy 13.

Ullrich-Turner Syndrome (n = 6)

Intracardiac abnormalities were observed in only two of the five cases where the heart was examined (Table V). However, in all six cases there was tubular hypoplasia of the ascending aorta and aortic isthmus (Fig. 9) with a significant decrease from normal in AoV, AoI and the ratio of AoV to PV but an increase in the ratio of AoV to AoI and Dad to AoI (Table II, Fig. 5).

The combined data from all four chromosomal abnormalities demonstrated a significant association between the degree of narrowing in AoI and nuchal translucency thickness (Fig. 10) ($r = -0.312$, $n = 91$, $P < 0.005$).

DISCUSSION

This study demonstrates the feasibility of recovering the fetal heart and great arteries for pathological examination even after surgical termination in the first trimester of pregnancy. The data confirm our previous findings that a high proportion of trisomy 21 fetuses have atrioventricular septal defects and narrowing of

Fig. 2. A scanning electron micrograph of the septal aspect of the right ventricle showing an atrioventricular septal defect type I (open circle). The right ventricular outflow tract has collapsed partially during processing of the specimen (arrow). Right atrium (A), common atrioventricular valve (v), crista supraventricularis (c). Scale bar: 500 μm [13 mm].

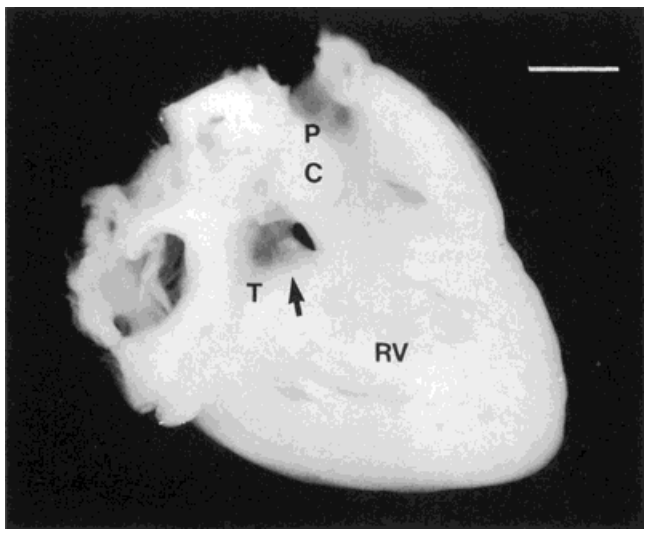

Fig. 3. Perimembranous ventricular septal defect (arrow) partially guarded by the septal leaflet of the tricuspid valve in a fetal heart from a 13-week trisomy 21 fetus. Septal leaflet of the tricuspid valve (T), crista supraventricular (C), pulmonary valve (P), right ventricle (RV). Scale bar: 1 mm [14mm].

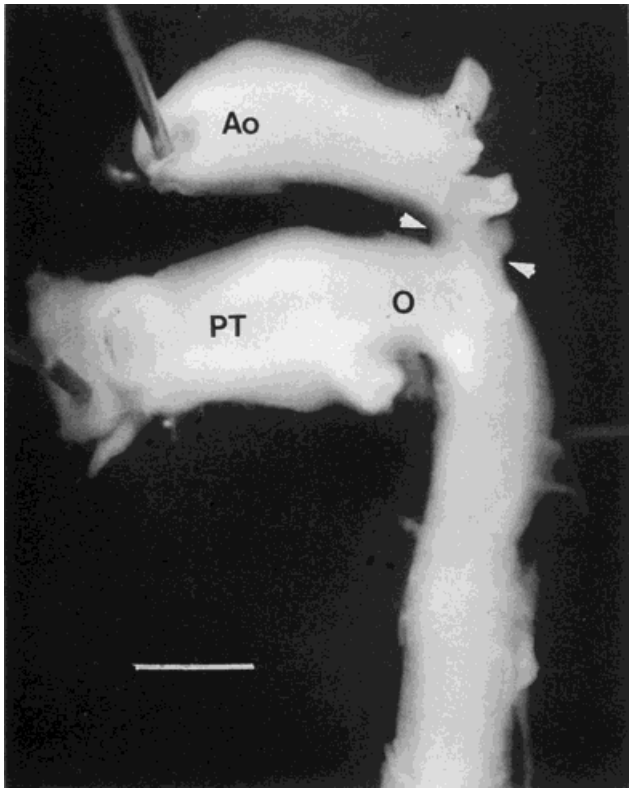

Fig. 4. The aorta (Ao), pulmonary trunk (PT) and Ductus arteriosus (open circle) from a trisomy 21 affected fetus at 14 weeks of gestation. The ascending aorta and the isthmus of the aorta (arrowheads) show some developmental delay. The aortic isthmus (arrowheads) is narrow compared to the distal ductus arteriosus, which is mildly dilated. Scale bar: 1 mm.

the aortic isthmus, whereas trisomy 18 is characterized by the presence of perimembrenous septal defects, polyvalvular disease, and narrowing of either the aortic isthmus or the pulmonary trunk [Hyett et al., 1995a,b,d]. Additionally, this study has examined fetuses with UTS, which is characterised by tubular hypoplasia of the aortic arch, and fetuses with trisomy 13, where common findings include ventricular or atrioventricular septal defects, agenesis of the semilunar valves and narrowing of the aortic isthmus or truncus arteriosus.

The high prevalence of cardiac abnormalities in trisomy 18 and trisomy 13 fetuses is consistent with data from echocardiographic studies of affected neonates [Balderston et al., 1990; Musewe et al., 1990] and postmortem studies of stillbirths or postnatal deaths [Matsuoka et al., 1983; Van Praagh et al., 1989]. Similarly, the strong association between UTS and coarctation of the aorta has been described previously in both pathological and clinical studies [Miyabara et al., 1989; Clark, 1984].

In contrast to trisomies 18 and 13 and UTS in trisomy 21 fetuses the prevalence of cardiac defects was higher than in postnatal echocardiographic studies [Hoe et al., 1990; Tubman et al., 1991]. A possible explanation for this apparent discrepancy is spontaneous intrauterine closure of some septal defects; in two of our cases the perimembranous ventricular septal defect was partly obliterated by the overlying septal leaflet of the tricuspid valve. Additionally, it is possible that there is a higher rate of intrauterine lethality in those trisomic fetuses with a septal defect than in those without [Hyett et al., 1996]. The impact of this potential for preferential miscarriage on the sensitivity of screening by maternal age and fetal nuchal translucency has been addressed previously by examining, first, the rate of fetal lethality between screening and termination of trisomic pregnancies, second, the evolution of nuchal translucency in trisomic fetuses when the parents choose to continue with the pregnancy, and third, the degree of reduction in the livebirth prevalence of trisomy 21 compared with the estimated prevalence based on the maternal age distribution of the population examined. Although such studies confirmed preferential miscarriage of fetuses with increased translucency, there was only a minor reduction in the sensitivity of the screening test, which was 80% [Snijders et al., 1996].

The finding of our study of an association between nuchal translucency thickness and the prevalence of defects in the great arteries and intracardiac anatomy is consistent with animal studies. The trisomy 16 mouse, which is considered to be a good animal model for human trisomy 21, has a combination of abnormalities of lymph vessels, cardiovascular malformations, and hypoplastic thymus that have been attributed to impaired migration of neural crest cells [Miyabara et al., 1989]. These cells migrate from the embryonic neural tube and play a central role in the development of the cardiovascular system [Besson et al., 1986]. There is increasing evidence that many neural crest-related cardiovascular defects may be genetically based

TABLE II. Mean Delta Values for Great Vessel Diameters in Chromosomally Abnormal Fetuses

	Trisomy 21			Trisomy 18			Trisomy 13			Turner syndrome		
Vessel segment	n	mean	SE	n	mean	SE	n	mean	SE	n	mean	SE
Aortic valve (AoV)	51	0.760**	0.186	26	0.336	0.281	13	−0.653*	0.189	5	−1.989**	0.243
Pulmonary valve (PV)	50	0.167	0.175	26	0.188	0.307	13	−0.821	0.707	5	0.026	0.472
Aortic isthmus (AoI)	48	−1.422**	0.197	25	−0.877*	0.336	12	−2.314**	0.432	6	−2.961**	0.148
Ductus arteriosus (Dad)	47	0.033	0.245	25	0.062	0.490	12	0.416	0.964	6	0.562	0.226
Ratio of AoV to PV	50	0.924**	0.291	26	0.836	1.005	13	3.040	2.843	5	−3.362**	0.721
Ratio of AoV to AoI	48	3.468**	0.399	25	2.143**	0.595	12	4.823**	1.185	5	4.191**	0.900
Ratio of Dad to AoI	45	3.458**	0.615	25	3.267	1.525	12	9.538**	2.652	6	13.903**	1.548

* $P < 0.05$; ** $P < 0.01$.

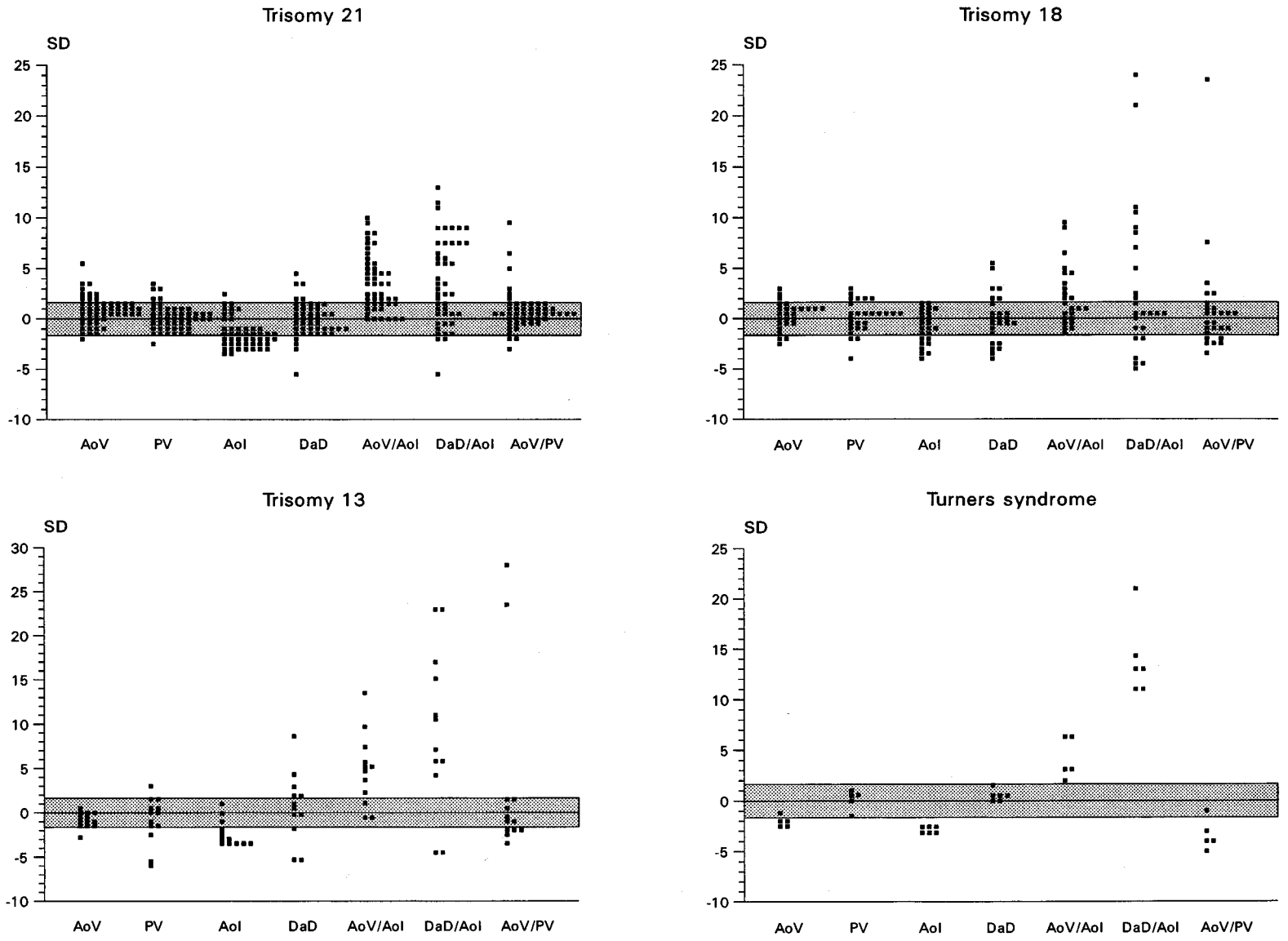

Fig. 5. Individual delta values for the aortic valve (AoV), pulmonary valve (PV), aortic isthmus (AoI), distal ductus arteriosus (DaD), and the ratios AoV:PV, AoV:AoI, and DaD:AoI shown for each chromosomal abnormality. The 10th and 90th centiles are also shown.

TABLE III. Cardiac Defects Identified by Pathological Examination of 29 Trisomy 18 Fetuses*

Case	NT (mm)	Septal defects	Valvular abnormalities	Great vessel abnormalities
1	1.5	Perimembranous ventricular	Bicuspid pulmonary and aortic valves	Dilated ascending aorta, dilated pulmonary trunk
2	1.5	None	Dysplastic tricuspid and mitral valves	
3	1.7	None	Dysplastic tricuspid valve	Normal
4	1.8	Perimembranous ventricular	None	Normal
5	2.2			Normal
6	3.1	Perimembranous ventricular	Bicuspid pulmonary valve, dysplastic tricuspid and mitral valves	Dilated aortic valve and ascending aorta, dilated pulmonary trunk
7	3.8	Perimembranous ventricular	Dysplastic tricuspid valve	Dilated pulmonary valve
8	5.0	Perimembranous ventricular	None	Normal
9	5.0	Perimembranous ventricular	Overriding aortic valve	Narrow ductus arteriosus
10	5.0	Perimembranous ventricular	Bicuspid pulmonary and aortic valves	Persistent LSVC
11	5.0	Perimembranous ventricular	Imperforate mitral valve, bicuspid aortic valve	Narrow aortic isthmus, dilated pulmonary trunk, pulmonary valve and ductus arteriosus, persistent LSVC
12	5.0	Perimembranous ventricular	Bicuspid, dysplastic pulmonary valve, dysplastic tricuspid valve	Narrow ductus arteriosus
13	5.0	Inlet and apical ventricular	Dysplastic tricuspid valve	
14	5.0	—	—	Narrow aortic isthmus and ductus arteriosus
15	5.5	—	—	Double aortic arch, narrow left aortic isthmus
16	5.7	—	—	Narrow aortic isthmus
17	6.0	Perimembranous ventricular	Bicuspid, dysplastic pulmonary valve, dysplastic tricuspid valve	Dilated aortic valve and ascending aorta
18	6.6	None	Dysplastic pulmonary and aortic valves	Narrow aortic isthmus, dilated pulmonary valve, pulmonary trunk and ductus arteriosus
19	6.8	—	—	Narrow ductus arteriosus
20	7.0	None	Imperforate pulmonary valve, bicuspid aortic valve, dysplastic tricuspid valve	Persistent LSVC
21	7.8	Perimembranous ventricular	Bicuspid aortic valve, agenesis pulmonary valve, dysplastic tricuspid and mitral valves	Dilated pulmonary valve, pulmonary trunk and ductus arteriosus
22	8.0	Perimembranous and muscular inlet ventricular	Bicuspid pulmonary and aortic valves, hypoplastic mitral valve, dysplastic tricuspid valve	Narrow aortic valve, ascending aorta and aortic isthmus, dilated ductus arteriosus, persistent LSVC
23	8.0	Perimembranous ventricular	Imperforate pulmonary valve, bicuspid aortic valve, dysplastic tricuspid aortic valve	Narrow pulmonary valve, pulmonary trunk and ductus arteriosus, dilated ascending aorta and aortic isthmus
24	8.0	Perimembranous ventricular	All valves dysplastic	Dilated ductus arteriosus, persistent LSVC
25	8.0	Perimembranous ventricular	Imperforate pulmonary valve	Narrow pulmonary valve, pulmonary trunk and ductus arteriosus, dilated ascending aorta and aortic isthmus, persistent LSVC
26	8.0	Perimembranous ventricular	Imperforate pulmonary valve, bicuspid aortic valve	Narrow pulmonary trunk and ductus arteriosus
27	8.1	—	—	Narrow aortic valve, ascending aorta and aortic isthmus
28	9.5	Perimembranous ventricular	None	Dilated aortic valve and ductus arteriosus
29	10.7	Perimembranous ventricular	Dysplastic tricuspid valve	Narrow ascending aorta and aortic isthmus, pesistent LSVC

* Cases are listed in order of thickness of the sonographic marker of nuchal translucency.

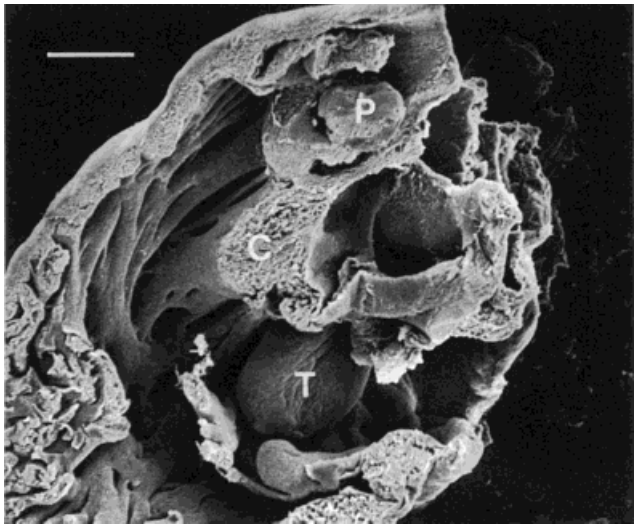

Fig. 6. A scanning electron micrograph of the parietal aspect of the right ventricle showing marked dysplasia of both the pulmonary (P) and tricuspid (T) valves in a trisomy 18 fetus at 12 weeks of gestation. Crista supraventricularis (C). Scale bar: 500 μm [14mm].

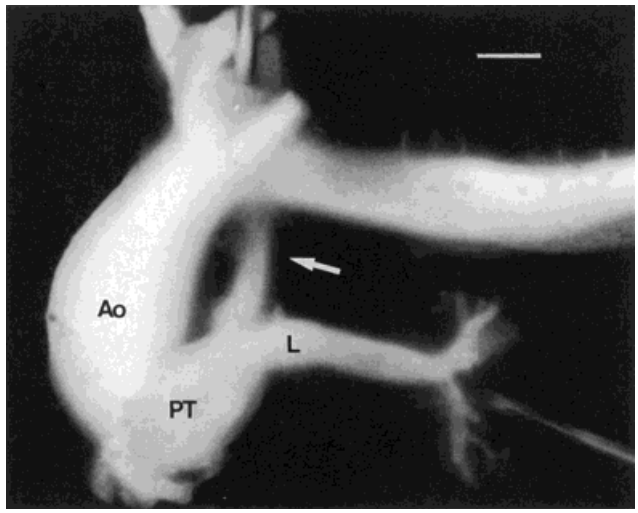

Fig. 7. A hypoplastic pulmonary trunk (PT) and ductus arteriosus (arrow) in a trisomy 18 fetus at 13 weeks of gestation. The left pulmonary artery (L) and ascending aorta (Ao) are dilated. Scale bar: 1 mm [11 mm].

TABLE IV. Cardiac Defects Identified by Pathological Examination of 17 Trisomy 13 Fetuses*

Case	NT (mm)	Septal defect	Valvular abnormalities	Great vessel abnormalities
1	2.0	None	Dysplastic tricuspid valve	Narrow ascending aorta and aortic isthmus
2	2.1	None	Bicuspid aortic valve	Narrow ascending aorta and aortic isthmus
3	3.0	Atrioventricular	Dysplastic common atrioventricular valve	—
4	3.8	None	Bicuspid aortic valve	Narrow ascending aorta and aortic isthmus, dilated ductus arteriosus
5	3.8	None	None	Narrow ascending aorta and aortic isthmus
6	4.1	Infundibular ventricular	Dysplastic tricuspid valve	Truncus arteriosus
7	4.8	Muscular ventricular	Agenesis pulmonary valve, bicuspid aortic valve	Dilated pulmonary trunk and ductus arteriosus
8	5.0	Perimembranous ventricular	Agenesis pulmonary valve, dysplastic tricuspid valve	Narrow aortic isthmus
9	5.6	Perimembranous ventricular	Imperforate pulmonary valve, atresia mitral valve	Hypoplastic pulmonary trunk and ductus arteriosus
10	6.2	Perimembranous ventricular	Imperforate pulmonary valve, dysplastic tricuspid valve	Hypoplastic pulmonary trunk and ductus arteriosus
11	6.3	—	Agenesis pulmonary valve	Narrow aortic isthmus, dilated ductus arteriosus
12	7.3	Atrioventricular	Dysplastic common atrioventricular valve	Narrow aortic isthmus
13	8.0	Infundibular ventricular	Dysplastic tricuspid valve	Truncus arteriosus
14	8.0	Perimembranous ventricular	None	Narrow ascending aorta and aortic isthmus
15	8.2	None	Agenesis aortic and pulmonary valves	—
16	9.2	Perimembranous ventricular	Dysplastic tricuspid valve	Truncus arteriosus
17	12.0	Perimembranous ventricular	Agenesis pulmonary valve	Narrow aortic isthmus

* Cases are listed in order of thickness of the sonographic marker of nuchal translucency.

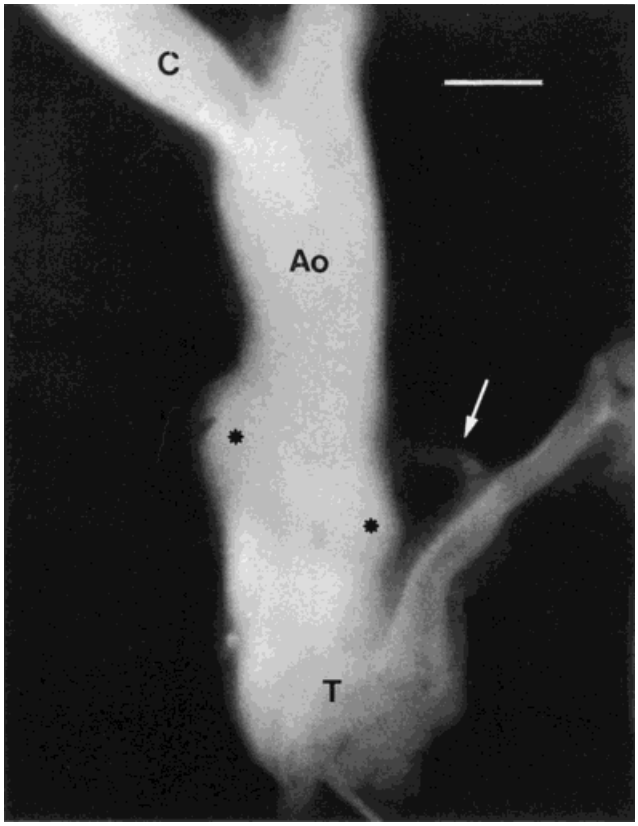

Fig. 8. Truncus arteriosus type I (T) in a fetus at 12 weeks of gestation. The right pulmonary artery is a tenuous vessel (arrow). The lateral bulges (*) are a positional fixation artifact. The carotid arteries have a common origin (C). Scale bar: 1 mm [13 mm].

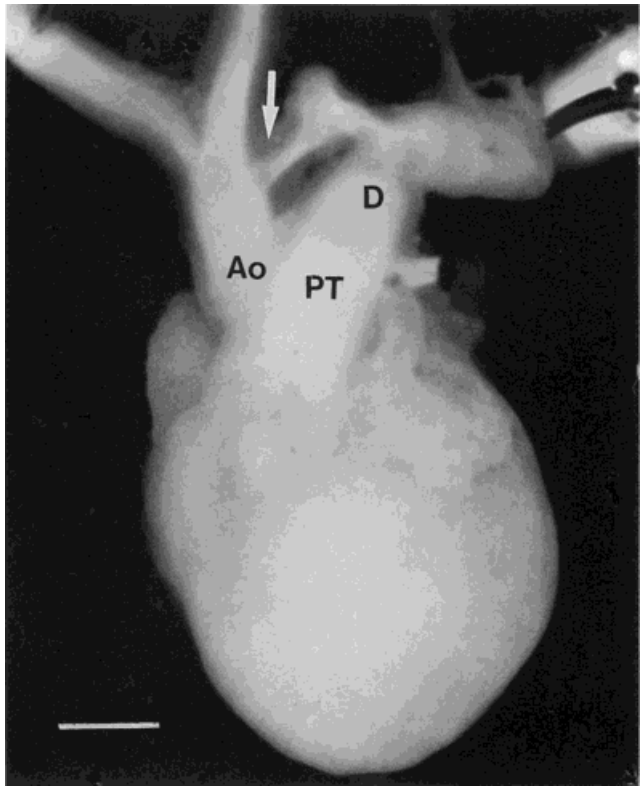

Fig. 9. The ascending aorta (Ao) is hypoplastic and the aortic arch (arrow) extremely hypoplastic in this 12-week fetus with Turner syndrome. The ductus arteriosus (D) is dilated. Pulmonary trunk (PT). Scale bar: 1 mm [13 mm].

[Halford et al., 1993]. The genetic mechanism whereby a series of different chromosomal defects interfere with neural crest cells to result in abnormalities of the aortic arch and cardiac defects, predominantly left sided, remains to be determined.

A consistent finding in all four types of chromosomal defects was relative narrowing of the aortic isthmus and an overall association between the degree of narrowing of the isthmus and translucency thickness. In trisomies 21 and 18, narrowing of the isthmus was associated with widening of the ascending aorta. Since blood flow is related to vessel diameter, widening of the ascending aorta and narrowing of the isthmus could result in overperfusion of the tissues of the head and neck leading to subcutaneous edema. We have previously shown that with advancing gestation there is differential growth in the diameter of the great vessels, and the diameter of the aortic isthmus increases more rapidly than the diameters of the aortic valve and distal ductus [Hyett et. al., 1995c]. Narrowing of the aortic isthmus was present in 50% of trisomy 21 fetuses, whereas the prevalence of coarctation of the aorta in affected neonates is only 2.5% [Hoe et al., 1990; Tubman et al., 1991]. Therefore, with increasing gestation, the hemodynamic consequences of narrowing of the isthmus may be overcome. This hypothesis could offer an explanation for the gestational age-related spontaneous resolution of nuchal translucency, e.g., abnormal nuchal fluid is ob-

TABLE V. Cardiac Defects Identified by Pathological Examination of 6 Turner Syndrome 13 fetuses*

Case	NT (mm)	Septal defect	Valvular abnormalities	Great vessel abnormalities
1	4.6	None	None	Tubular hypoplasia of the aortic arch
2	7.4	—	—	Tubular hypoplasia of the aortic arch
3	8.3	Muscular ventricular septal defect	Bicuspid aortic valve	Tubular hypoplasia of the aortic arch
4	8.5	None	None	Tubular hypoplasia of the aortic arch
5	8.8	None	None	Tubular hypoplasia of the aortic arch
6	9.5	None	Bicuspid aortic valve	Tubular hypoplasia of the aortic arch

* Cases are listed in order of thickness of the sonographic marker of nuchal translucency.

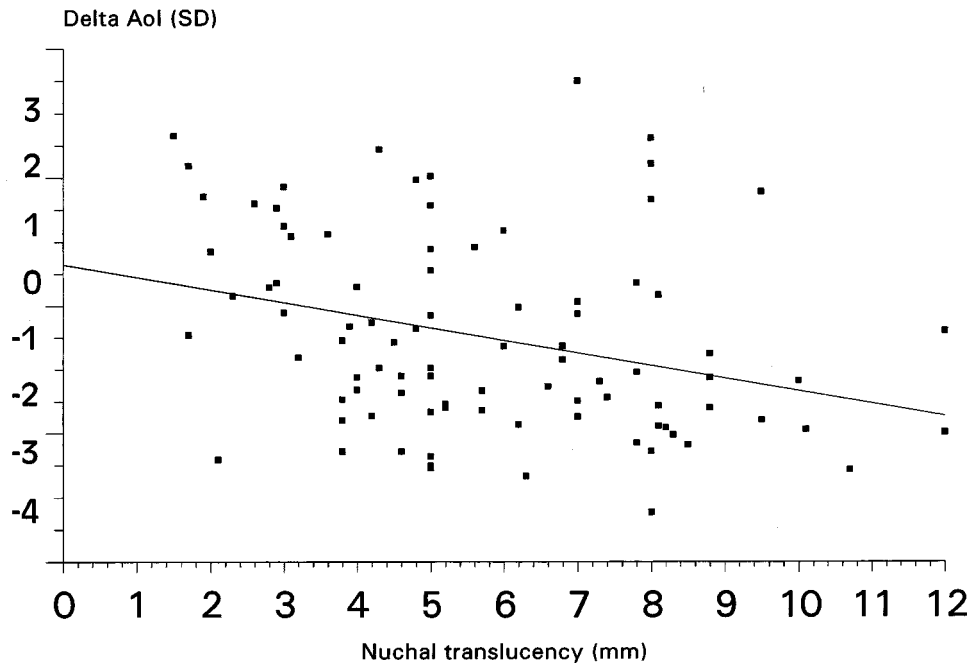

Fig. 10. Relationship between the degree of narrowing in the aortic isthmus (delta AoI) and nuchal translucency thickness for all chromosomal abnormalities.

served in 80% of trisomy 21 fetuses at 11 weeks of gestation [Pandya et al., 1995], but in only 30% of cases at 20 weeks [Nicolaides et al., 1992].

In trisomy 13 and UTS, narrowing of the isthmus was accompanied by narrowing of the ascending aorta and therefore development of increased nuchal translucency cannot be explained by overperfusion of the head and neck. In the case of UTS, increased nuchal translucency is thought to represent overdistention of the jugular lymphatic sacs as a consequence of failure of communication with the internal jugular vein [Van der Putte, 1977]. Clark et al. [1984] suggested that the associated cardiovascular malformations, primarily coarctation of the aorta and other defects in the spectrum of left heart obstruction, are the consequence of altered intracardiac blood flow due to compression of the ascending aorta by the distended intrathoracic lymphatic channels.

This study has demonstrated the feasibility of undertaking pathology studies of the heart and great arteries in early pregnancy, and the findings illustrate a high prevalence of defects in chromosomally abnormal fetuses.

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